

WHAT IS CLAIMED IS:

1. A method of identifying an agent that alters the level of surface expression of a protein in a mammalian cell, said method comprising:

- a) preparing a first medium containing mammalian cells that express said protein;
- b) adding to said first medium containing mammalian cells an effective amount of a candidate agent;
- c) incubating said cells in the presence of said candidate agent for a sufficient period of time;
- d) treating said cells with an effective amount of a fixative;
- e) adding to said first medium containing mammalian cells an effective amount of at least one antibody which binds to said protein; and
- f) determining the level of binding of said antibody to said protein with said candidate agent, wherein a change in said level of binding relative to control indicates that said candidate agent alters the level of surface expression of said protein.

2. The method according to claim 1, wherein step (e) comprises adding an effective amount of at least one primary antibody followed by an effective amount of at least one secondary antibody, wherein said primary antibody binds to at least one extracellular epitope of said protein and said secondary antibody binds to said first antibody.

3. The method according to claim 1, wherein said level of binding is measured by fluorescence, luminescence, radioactivity, absorbance or a combination of two or more thereof.

4. The method according to claim 1, wherein said protein is an integral membrane protein.

5. The method according to claim 2, wherein said at least one extracellular epitope comprises a wild-type epitope.

6. The method according to claim 2, wherein said at least one extracellular epitope contains a tag.

7. The method according to claim 6, wherein said extracellular tag replaces at least a portion of an extracellular domain of said protein.

8. The method according to claim 7, wherein said extracellular tag is inserted in an extracellular domain of said protein.

9. The method according to claim 6, wherein said extracellular tag comprises a hemagglutinin (HA) tag.

10. A method of identifying an agent that alters the level of expression of a protein in a mammalian cell, said method comprising:

- a) preparing a first medium containing mammalian cells that express said protein;
- b) adding to said first medium containing mammalian cells an effective amount of a candidate agent;
- c) incubating said cells in the presence of said candidate agent for a sufficient period of time;
- d) treating said cells with a fixative followed by a permeabilizing agent;
- e) adding to said first medium containing mammalian cells an effective amount of at least one antibody which binds to said protein; and
- f) determining the level of binding of said antibody to said protein with said candidate agent, wherein a change in said level of binding relative to control indicates that said candidate agent alters the level of expression of said protein.

11. The method according to claim 10, wherein step (e) comprises adding an effective amount of at least one primary antibody followed by an effective amount of at least one secondary antibody, wherein said primary antibody binds to at least one epitope of said protein and said secondary antibody binds to said first antibody.

12. The method according to claim 10, wherein said level of binding is measured by fluorescence, luminescence, radioactivity, absorbance or a combination of two or more thereof.

13. The method according to claim 10, wherein said protein is an integral membrane protein.

14. The method according to claim 11, wherein said at least one epitope comprises a wild-type epitope.

15. The method according to claim 11, wherein said at least one epitope contains a tag.

16. The method according to claim 15, wherein said tag replaces at least a portion of a domain of said protein.

17. The method according to claim 15, wherein said tag is inserted in a domain of said protein.

18. The method according to claim 15, wherein said tag comprises a hemagglutinin (HA) tag.

19. The method according to claim 1 or 10, wherein said primary antibody and/or said secondary antibody is coupled to an enzyme.

20. The method according to claim 1 or 10, wherein said enzyme is selected from the group consisting of peroxidases, luciferases, alkaline phosphatases, glucose oxidases, beta-galactosidases and mixtures of two or more thereof.

21. A method of identifying a peptide that alters the level of expression of an integral membrane protein in a mammalian cell, said method comprising:

- a) preparing a first medium containing mammalian cells that express said protein;
- b) adding to said first medium containing mammalian cells a retroviral expression library;
- c) adding to said first medium containing mammalian cells an effective amount of at least one antibody that binds to at least one extracellular epitope of said protein;
- d) adding to said medium a fluorescently tagged secondary antibody; and
- e) sorting said mammalian cells based on fluorescence.

22. The method according to claim 21, wherein said protein is an ion channel.

23. The method according to claim 21, wherein said at least one epitope comprises a wild-type epitope.

24. The method according to claim 21, wherein said at least one epitope contains a tag.

25. The method according to claim 24, wherein said tag replaces at least a portion of a domain of said protein.

26. The method according to claim 24, wherein said tag is inserted in a domain of said protein.

27. The method according to claim 24, wherein said tag comprises a hemagglutinin (HA) tag.

28. The method according to claim 21, wherein said primary antibody and/or said secondary antibody is coupled to an enzyme.

29. The method according to claim 21, wherein said enzyme is selected from the group consisting of peroxidases, luciferases, alkaline phosphatases, glucose oxidases, beta-galactosidases and mixtures of two or more thereof.

30. The method according to claim 6, 15 or 24, wherein said tag in said extracellular epitope is the only tag present on said protein.

31. The method according to claim 1 or 10, wherein said protein contains a fluorescent tag.

32. The method according to claim 31, wherein said tag is selected from the group consisting of Green Fluorescent Protein, Red Fluorescent Protein, Blue Fluorescent Protein and amino acid sequences which selectively bind a molecule which has a detectable characteristic.

33. The method according to claim 32, wherein said tag replaces at least a portion of an intracellular domain of said protein.

34. The method according to claim 32, wherein said tag is inserted in an intracellular domain of said protein.

35. The method according to claim 33 or 34, wherein said tag in said intracellular domain is the only tag present on said protein.